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Review Article

Recent Advances in Determinations of Nanomedicine and Nanotechnology

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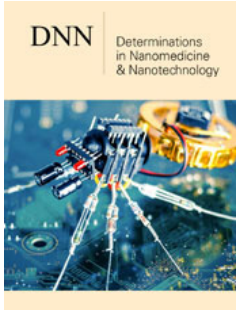

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Abstract

The application of nanomedicine in nanotechnology is offering many exciting possibilities in healthcare. Engineered nanoparticles have the potential to rapid drug delivery and to revolutionize the diagnosis and the therapy of several diseases e.g. cardiovascular disease (atherosclerosis), atherosclerotic plaque imaging particularly by targeted delivery of anticancer drugs and imaging contrast agents. In short nanotechnology offers emerging therapeutic strategies, which may have advantage over classical treatments for several diseases and help diagnosis of the disease.

Keywords: Nanotechnology; Consolidation; Deformation; Materials

Introduction

Scientific understanding through the millennia has come from studying things first as they present themselves in the natural world and then from studying and understanding their subcomponents at ever smaller scales and then finer levels of detail. Nanotechnology is a broad field of modern sciences and also engineering which creates potentially the endless possibilities. This term was first time used in 1974 by the Japanese scientist Norio Taniguchi according to him the definition of nanotechnology was that it mainly consists of the processing of separation, consolidation, and deformation of materials by one atom or one molecule" [1]. The prefix "nano" refers to one-billionth. So, the term nanotechnology (nanoscience) is now commonly used to refers to the creation of new objects with nanoscale dimensions between 1.0 and 100.0nm or one billion of meter (10-9m) [2-4]. The term also conceptually implies the ability to manipulate individual atoms or molecules as the building blocks of man-made nanoscale structures [5]. Nowadays, nanotechnology is an interdisciplinary field involving issues of precision mechanics, biology, electronics, materials science, physics, chemistry, electromechanical systems as well as the use of biomedicine and bioengineering for drug or gene therapy application.

Nanotechnology opens the new ways of approaching desired goals. For that, both scientist and engineers use different tools and methodology. There are many reasons why scientists and engineers with their diverse interests as well as strong backgrounds including above mentioned fields have converged their interest to understand and works with things on nanoscale. Hence, they are seeking to exploit unique nanoscale properties to create novel new products and to solve problems of longstanding interest. Particularly biological systems are inherently composed of nanoscale building blocks like, the width of DNA molecule is approximately 2.5nm [6] as well as the dimensions of most proteins are in the range of 1.0 to 15.0/20.0nm, and the width of cell membranes is in the range of 6-10nm [6,7]. So, nanotechnology has been particularly influencing the field of medicine from microfluidics, drug delivery, nan-biotechnology, biosensors, and microarrays to tissue micro-engineering [8]. Inherently, most research in molecular biology already takes place on a nanoscale.

General interest in nanotechnology beyond biological system is also enormous and stems from the fact that the properties of nanoscale materials and objects are quite different from the properties of the same chemical materials created with larger dimensions, as a result of fundamental principles of quantum physics [4,9] e.g. the strength, melting & boiling point, color, electrical conductivity, magnetic and optical properties all are potentially affected.

Nanomedicine is the application of nanotechnology to health and medicine, in monitoring, diagnosing, preventing, repairing or curing diseases and damaged tissues in biological systems. It involves a wide range of scientific disciplines, including physics, chemistry, engineering, biology, and medical this term was first mentioned in the book "Unbounding the Future". The Nanotechnology Revolution in 1991 [10]. During the past 20years, with the advancement of knowledge of the human genome, detailed molecular level understanding of the diseases, the development of sophisticated technologies for nanoscale manipulation and analysis of matter, nanomedicine has undergone an explosive growth in the United States and worldwide [11]. Nanomedicine has made a rapid and broad impact on healthcare. There are more than 200 nanomedicine products that have been either approved or are under clinical investigation [12]. Nanomedicine, with its advantages of rapid diagnosis, high sensitivity and high accuracy, has aroused extensive interest of researchers, as the cornerstone of nanomedicine, nanomaterials achieve extra attention and rapid development.

To distinguish with which approach we faced, the two terms has been introduce: top-down and bottom-up approaches for the synthesis of nanoparticles. Briefly, top-down refers to the methods of nano-objects fabrication for which macroscopic tools are hired, such as deposition, etching, machining, etc.; whereas bottom-up to methods where the structures are built up atom-by-atom or molecule-by-molecule. In some sense, this represents a "U-turn" in scientific inquiry. The aim of this review is to highlight the recent scientific advances and, on this basis, to outline the potential use of nanoscience and nanomedicine for biological system.

Nanotechnology and Nanomedicines in Clinical Utility

It is envisioned that the nanotechnology and nanomedicine approaches will enables the establishment of patient specific "personalized medicine" in the near future. As the clinical success of nanoparticles are dependent on their

A. Stability and time in circulation,

B. Ability to cross physiological barriers and to gain access to the affected anatomic sites,

C. Bioavailability at the disease site, and

D. Safety profile [13]. Improving these characteristics should contribute to enhance the efficacy of nanomedicines, consequently helping to bring them into mainstream cancer treatment.

Therefore, the two major disease areas that have undergone radical refinement in treatment approaches via nanomedicine strategies are cancer and vascular pathologies. The quest to enhance the efficacy of nano-therapeutics is expected to follow several parallel paths. We expect it to involve the following:

A. Developing approaches to enhance nanoparticle tumor accumulation and penetration;

B. Expanding the "toolbox" of molecules that are being delivered using nanoparticles and thus, enabling therapies that are not accessible to conventional drug delivery;

C. Identifying "niche" cancer interventions that are uniquely positioned to benefit from nanotechnology; and finally

D. Improving designs of clinical trials involving nano-therapeutics [13].

Determinations of Nanotechnology & Nanomedicine in Biological System

Nanotechnology for drug delivery

The potential of eliminating a tumorous outgrowth without any collateral damage through nanomaterial-based drug delivery has created significant interest and nanoparticles form the basis for bio-nanomaterials [5] and major efforts in designing drug delivery systems are based on functionalized nanoparticles [14,15]. So, the most promising application of nanomaterials is the promise of targeted, site-specific drug delivery. Initially, scientist was devised as carriers for vaccines and anticancer drugs [16] and then the nanometer size ranges may significantly enhance the drug delivery by affecting the bio-distribution and toxic dynamics of drugs [17,18]. This can make *in vivo* delivery of many types of drugs which pose serious delivery problems, a relatively easy task [19].

Functionalizing or modifying nanoparticles to deliver drugs through the blood brain barrier for targeting brain tumors can be regarded as a brilliant outcome of nanoscience [20]. For example, doxorubicin does not cross the blood-brain barrier, but its integration with polysorbate-80 modified poly butyl cyanoacrylate nanoparticles can increase its delivery to the brain to its significant extent [20]. Due to their shape, size and functionality, nanoparticle systems play a vital role in creation of DNA delivery vectors [21]. It can penetrate deep into tissues and are absorbed by the cells efficiently [22]. Nano-sized colloidal carriers of drugs can be regarded as an advanced development in pharmacotherapy [23]. They act as potential carriers for several classes of drugs like anti-cancer, anti-hypertensive and hormones, etc. [24]. Submicron colloidal particles have been used as nanoparticles for the purpose of drug delivery [25] and also used for the diagnosis of diseases [19]. Nanotechnology have widened the scope of pharmacokinetics for insoluble drugs. For example, the trans-retinoic acid nanoparticle coated by $CaCO_3$ was developed as a new drug delivery system, which on spray drying formed aggregates. The aggregates thus formed were found to re-disperse in water, which stimulated insulin secretion from islets [26].

Liposome & lipid-based nanoparticles

The first nanoparticle platform in nanomedicine was liposome. Liposome and lipid nanoparticle formulations are excellent delivery

vehicles for nucleic acid therapeutics, such as gene therapy agents and small interfering RNAs (siRNAs) [27] and also utilized in drug delivery for both small molecules as well as protein drugs [28,29] the four decades, research in liposome and lipid nanoparticle drug delivery led to the development of the first FDA approved nanomedicine, DOXIL, as well as 12 additional therapeutics [30]. Moreover, there are 30 liposomal or lipid nanoparticle-based therapeutics currently under clinical investigation.

Liposomes as drug delivery system: A widely used approach is the creation of "stealth" liposomes by adding polyethylene glycol (PEG) groups to the exterior part of the liposomes, also termed as PEGylation, [31] thus protecting them from phagocytosis and prolonging plasma half-life. Release of the drug is usually achieved via cleavage of the PEG-liposome bond under specific environmental stimuli [32,33]. Drug release was achieved by endocytosis of the liposome and release of the drug. Use of liposomes resulted in low drug dosage as well as fewer systemic side effects [34].

Cell imaging and therapeutic applications

Cardiovascular disease or atherosclerosis (CVD) is the leading cause of death and disability in both genders in the developed and developing world and the primary clinical endpoints are coronary heart disease and stroke. The major underlying pathology is an atherosclerosis leading to lipid accumulation in the arterial wall and plaque formation. Nanomedicine has also contributed to the field of atherosclerotic plaque imaging and help diagnosis of the disease. Psarros et al. [35] summarize the increasing evidence of nanomedicines for targeted drug delivery and plaque imaging [36]. A range of molecular and cellular imaging [37,38] have been applied to imaging techniques, such as ultrasound (US), positron emission tomography (PET), MRI, single photon emission computed tomography (SPECT) and computed tomography (CT) [39]. The materials used to enhance imaging of inflammation and atherosclerotic plaques including liposomes polyamidoamine (PAMAM) and diaminobutane (DAB) dendrimers [40-42] gold nanoparticles [43,44] silver nanoparticles [45] quantum dots [46] iron microparticles [47] or dextran coated ultra-small particles of iron oxide (USPIO) [48].

Previous development of nanotechnology systems tended to focus on very specific applications while, recent development has placed more emphasis on the dual application for both therapeutic and diagnostic purposes. These products with dual applications are termed "theranostic" nanoparticles and are able to be delivered to a specific pathological area for imaging while simultaneously act as therapeutic agents. In addition, the ability to guide evaluation of the effects can provide critical information about the efficacy and efficiency of treatment.

Ex vivo and in-vivo biomarker detection

Biomarkers include circulating molecules that can provide diagnostic or prognostic value to a disease state. Biomarkers have become progressively powerful tools for the early detection of several disorders, enabling early and effective treatment of diseases [49]. The ideal biomarker should have high selectivity, sensitivity, and specificity and can be performed at a relatively low cost [49]. Nanotechnology is a promising tool in the field of biomarker discovery. The unique properties of nanomaterials can be fully utilized to in order to enhance detection of existing or novel biomarkers via the development of new devices. Cui et al. [50] reported the use of nanowires for the detection of pH variations, Ca^{2+} ion concentration, measurements of trace chemical, and biological molecules. Ability to measure such low quantities of substances offers great potential for accurate early diagnosis. The use of a micro-electro-mechanical system combined with nanoparticles has also improved sensitivity in detection of several existing biomarkers of AMI [51]. Nanotechnology not only offers capabilities for *ex vivo* but also for *in vivo* detection of biomarkers. There has been report of nano-sensors, which can be implanted into the coronary artery and the epicardium [52]. These sensors were able to detect of several cations such as H^+, Ca^{2+}, Na^+ and K^+ *in vivo*, while simultaneously monitoring the role of K^+ and H^+ ion activity in MI. There have also been reports of nano-sensors for the detection of NO in endothelial cells [53] and the detection of oxidized LDL [54].

Physiological parameters detection

Multipurpose nanosized, sensors are being developed to detect almost everything from physiological parameters such as blood pressure, temperature, heart and respiration rates, etc. to toxic compounds [55]. The implantable sensor once swallowed or implanted will continue to send data throughout the life of the animal and later after slaughter to track animal products.

Blood estradiol detection in animal breeding

The management of the animal breeding is an expensive and time-consuming problem for dairy and swine farmers. The proposed solution under study is a nanomaterial such as nanotube implanted under the skin to determine the real time measurement of blood estradiol changes. The nanotubes [56] are used as a source of tracking estrus in animals because of the fact that as the nanotubes have the capacity to bind and detect the estradiol antibody at the time of estrus by near infrared fluorescence. The signal from this sensor will be incorporated as a part of a central monitoring and control system to actuate breeding. The natural follow up would be to have an implanted nano-capsule of semen triggered on demand to fertilize an egg.

Conclusion

Over the last few years there have been tremendous advances in the field of nanotechnology and nanomedicine, New nanomaterials and techniques are becoming available to improve bioavailability, drug loading capacity and specific tissue targeting efficiency, as well as to cell imaging, biomarker detection. The range of possible applications of nanotechnology in cardiovascular medicine is rapidly expanding, providing promising options in the treatment of atherosclerosis (through targeted drug delivery) but also in atherosclerotic plaque imaging. Therefore, nanoscience and nanomedicine may evolve into a valuable tool in the battle against biological system in the near future.

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